



## LISTING OF CLAIMS

1-23 (cancelled)

24. (new) A method for limiting the risks of cardiovascular disturbances and/or the risks of organ and/or tissue toxicity in the treatment of a living animal body afflicted with disorders which may be treated by double inhibition of serotonin (5-HT) and norepinephrine (NE) reuptake, said method comprising administering to the living animal body an effective amount of a mixture of enantiomers of milnacipran (Z(+)2-(amino methyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide) and/or of at least one of its metabolites, as well as their pharmaceutically-acceptable salts, such mixture being enriched in the (1S,2R) enantiomer.
25. (new) The method of claim 24, wherein the cardiovascular disturbance corresponds to an increase in blood pressure and/or an increase in heart rate.
26. (new) The method of claim 25, wherein the increase in blood pressure corresponds to an increase in diastolic blood pressure.
27. (new) The method according to claim 24, wherein the organ toxicity is cardiac toxicity and the tissue toxicity is hepatic and/or renal toxicity.
28. (new) The method according to claim 24, wherein the (1S,2R) enantiomer of milnacipran is the hydrochloride of Z-(1S,2R)-2-(aminomethyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide (F2695).
29. (new) The method according to claim 24, wherein the metabolite is selected from:
  - o the hydrochloride of Z-phenyl-1-aminomethyl-2-cyclopropane carboxylic acid (F1567),
  - o phenyl-3 methylene-3-4-pyrrolidone-3 (F1612),
  - o the hydrochloride of Z-(para-hydroxyphenyl)-1 diethylaminocarbonyl-1 aminomethyl-2 cyclopropane (F2782),
  - o the oxalic acid of Z-phenyl-1-ethylamino carbonyl-1 aminomethyl-2 cyclopropane (F2800), and

- the hydrochloride of Z-phenyl-1 aminocarbonyl-1 aminomethyl-2 cyclopropane (F2941).

30. (new) The method according to claim 24, wherein the mass/mass ratio between the (1S,2R) enantiomer and the (1R,2S) enantiomer in the mixture is greater than 95:5 ((1S,2R):(1R,2S)).

31. (new) The method according to claim 24, wherein the mass/mass ratio between the (1S,2R) enantiomer and the (1R,2S) enantiomer in the mixture is greater than 99:1 ((1S,2R):(1R,2S)).

32. (new) The method according to claim 24, wherein the mass/mass ratio between the (1S,2R) enantiomer and the (1R,2S) enantiomer in the mixture is greater than 99.5:0.5 ((1S,2R):(1R,2S)).

33. (new) The method according to claim 24, wherein the mixture of enantiomers is substantially pure in the hydrochloride of Z-(1S,2R)-2-(aminomethyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide (F2695).

34. (new) The method according to claim 24, wherein the mixture of enantiomers is substantially pure in the hydrochloride of Z-(1S,2R)-(para-hydroxyphenyl)-1-diethylaminocarbonyl-1-aminomethyl-2-cyclopropane.

35. (new) The method according to claim 24, wherein the disorder or condition is selected from depression, bi-polar disease, schizophrenia, generalised anxiety, morose and marasmic states, stress-related diseases, panic attacks, phobias, obsessive-compulsive disorders, behavioural disorders, oppositional disorders, post-traumatic stress disorder, depression of the immune system, fatigue and the associated pain syndromes, chronic fatigue syndrome, fibromyalgia, and other functional somatic disorders, autism, disorders characterised by attention deficit due to general health status, attention disorders due to hyperactivity, eating disorders, neurotic bulimia, neurotic anorexia, obesity, psychotic disorders, apathy, migraine, pain, irritable bowel syndrome, cardiovascular diseases, neuro-degenerative diseases and the associated anxiety-depressive syndromes (Alzheimer's disease, Huntington's chorea, Parkinson's disease), urinary incontinence, drug addiction.

36. (new) The method of claim 35, wherein depression is selected from deep depression, resistant depression, depression in the elderly, psychotic depression, depression induced by treatments with interferon, depressive state, manic-depressive syndrome, seasonal depressive episodes, depressive episodes related to general health status, depression related to mood-altering substances.
37. (new) The method of claim 36, wherein the (1S,2R) enantiomer of milnacipran is the hydrochloride of Z-(1S,2R)-2-(aminomethyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide (F2695).
38. (new) The method of claim 35, wherein phobia is agoraphobia.
39. (new) The method of claim 35, wherein pain is chronic pain.
40. (new) The method of claim 35, wherein the cardiovascular disease is selected from anxiety-depressive syndrome in myocardial infarct or in hypertension.
41. (new) The method of claim 35, wherein the urinary incontinence is selected from urinary incontinence related to stress and enuresis.
42. (new) The method of claim 35, wherein the drug addiction is selected from anxiety addiction to tobacco, to nicotine, to alcohol, to narcotics, to drugs, and to an analgesic used in weaning-off from these addictive states.
43. (new) The method according to claim 24, wherein the living animal body is selected from children, the elderly, patients with hepatic and/or renal insufficiency, patients receiving treatment that induces hepatic or renal organ and/or tissue toxicity, patients receiving treatment for a heart condition, patients receiving treatment that induces cardiovascular side-effects, and patients having a history of cardiovascular disease and/or suffering from cardiovascular disorders.
44. (new) The method according to claim 43, wherein the history of cardiovascular disease and/or cardiovascular disorders are chosen among myocardial infarct, cardiac rhythm disorders (tachycardia, bradycardia, palpitations), blood pressure disorders (hypo- or hypertensive patients) and heart disease.
45. (new) A method for limiting the risks of cardiovascular disturbances and/or the risks of organ and/or tissue toxicity in the treatment of a living animal body

afflicted with depression, which comprises administering to the living animal body :

a) a mixture of enantiomers enriched in the (1S,2R) enantiomer of milnacipran and/or of at least one of its metabolites as well as their pharmaceutically-acceptable salts, and

b) at least one active compound selected from the psychotropics, in particular antidepressants, and antimuscarinic agents,

as associated products for use simultaneously, separately or staggered in time.

46. (new) The method according to claim 45, wherein the depression is selected from deep depression, resistant depression, depression in the elderly, psychotic depression, depression induced by treatment with interferon, depressive state, manic-depressive syndrome, seasonal depressive episodes, depressive episodes related to general health status, depressive episodes related to mood-altering substances.

47. (new) A method for limiting the risks of organ and/or tissue toxicity in the treatment of a living animal body afflicted with conditions or disorders which may be treated by double inhibition of serotonin (5-HT) and norepinephrine (NE) reuptake, which comprises administering to the living animal body:

a) a mixture of enantiomers enriched in the (1S,2R) enantiomer of milnacipran and/or of at least one of its metabolites as well as their pharmaceutically-acceptable salts, and

b) at least one other active substance selected from the active compounds that induce organ toxicity and the active compounds that induce cell toxicity, in particular hepatic and/or renal,

as associated products for use simultaneously, separately or staggered in time.

48. (new) A method for limiting the risks of cardiovascular disturbances in the treatment of a living animal body afflicted with conditions or disorders which may be treated by double inhibition of serotonin (5-HT) and norepinephrine (NE) reuptake, which comprises administering to the living animal body:

a) a mixture of enantiomers enriched in the (1S,2R) enantiomer of milnacipran and/or of at least one of its metabolites as well as their pharmaceutically-acceptable salts, and

b) at least one other active substance selected from the active compounds that induce cardiovascular side-effects,

as associated products for use simultaneously, separately or staggered in time.

49. (new) A method for treating or preventing conditions or disorders by double inhibition of serotonin (5-HT) and norepinephrine (NE) reuptake in a living animal body, while limiting the risks of cardiovascular disturbances and/or the risks of organ and/or tissue toxicity, which comprises administering to the living animal body an effective amount of a mixture of enantiomers of milnacipran (*Z*( $\pm$ )-2-(amino methyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide) and/or of at least one of its metabolites, as well as their pharmaceutically-acceptable salts, such mixture being enriched in the (1S,2R) enantiomer.

50. (new) The method of claim 49, wherein the cardiovascular disturbance corresponds to an increase in blood pressure and/or an increase in heart rate.

51. (new) The method of claim 50, wherein the increase in blood pressure corresponds to an increase in diastolic blood pressure.

52. (new) The method of claim 49, wherein the organ toxicity is cardiac toxicity and the tissue toxicity is hepatic and/or renal toxicity.

53. (new) The method of claim 49, wherein the (1S,2R) enantiomer of milnacipran is the hydrochloride of *Z*-(1S,2R)-2-(aminomethyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide (F2695).

54. (new) The method of claim 49, wherein the metabolite is selected from:

- the hydrochloride of *Z*-phenyl-1-aminomethyl-2-cyclopropane carboxylic acid (F1567),
- phenyl-3 methylene-3-4-pyrrolidone-3 (F1612),
- the hydrochloride of *Z*-(para-hydroxyphenyl)-1 diethylaminocarbonyl-1 aminomethyl-2 cyclopropane (F2782),
- the oxalic acid of *Z*-phenyl-1-ethylamino carbonyl-1 aminomethyl-2 cyclopropane (F2800), and

- the hydrochloride of Z-phenyl-1 aminocarbonyl-1 aminomethyl-2 cyclopropane (F2941).

55. (new) The method of claim 49, wherein the mass/mass ratio between the (1S,2R) enantiomer and the (1R,2S) enantiomer in the mixture is greater than 95:5 ((1S,2R):(1R,2S)).

56. (new) The method of claim 49, wherein the mass/mass ratio between the (1S,2R) enantiomer and the (1R,2S) enantiomer in the mixture is greater than 99:1 ((1S,2R):(1R,2S)).

57. (new) The method of claim 49, wherein the mass/mass ratio between the (1S,2R) enantiomer and the (1R,2S) enantiomer in the mixture is greater than 99.5:0.5 ((1S,2R):(1R,2S)).

58. (new) The method of claim 49, wherein the mixture of enantiomers is substantially pure in the hydrochloride of Z-(1S,2R)-2-(aminomethyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide (F2695).

59. (new) The method of claim 49, wherein the mixture of enantiomers is substantially pure in the hydrochloride of Z-(1S,2R)(para-hydroxyphenyl)-1-diethylaminocarbonyl-1-aminomethyl-2-cyclopropane.

60. (new) The method of claim 49, wherein the disorder or condition is selected from depression, bi-polar disease, schizophrenia, generalised anxiety, morose and marasmic states, stress-related diseases, panic attacks, phobias, obsessive-compulsive disorders, behavioural disorders, oppositional disorders, post-traumatic stress disorder, depression of the immune system, fatigue and the associated pain syndromes, chronic fatigue syndrome, fibromyalgia, and other functional somatic disorders, autism, disorders characterised by attention deficit due to general health status, attention disorders due to hyperactivity, eating disorders, neurotic bulimia, neurotic anorexia, obesity, psychotic disorders, apathy, migraine, pain, irritable bowel syndrome, cardiovascular diseases, neuro-degenerative diseases and the associated anxiety-depressive syndromes (Alzheimer's disease, Huntington's chorea, Parkinson's disease), urinary incontinence, drug addiction.

61. (new) The method of claim 60, wherein depression is selected from deep depression, resistant depression, depression in the elderly, psychotic depression, depression induced by treatments with interferon, depressive state, manic-depressive syndrome, seasonal depressive episodes, depressive episodes related to general health status, depression related to mood-altering substances.
62. (new) The method of claim 61, wherein the (1S,2R) enantiomer of milnacipran is the hydrochloride of Z-(1S,2R)-2-(aminomethyl)-N,N-diethyl-1-phenylcyclopropanecarboxamide (F2695).
63. (new) The method of claim 60, wherein phobia is agoraphobia.
64. (new) The method of claim 60, wherein pain is chronic pain.
65. (new) The method of claim 60, wherein the cardiovascular disease is selected from anxiety-depressive syndrome in myocardial infarct or in hypertension.,
66. (new) The method of claim 60, wherein the urinary incontinence is selected from urinary incontinence related to stress and enuresis.
67. (new) The method of claim 60, wherein the drug addiction is selected from anxiety addiction to tobacco, to nicotine, to alcohol, to narcotics, to drugs, and to an analgesic used in weaning-off from these addictive states.
68. (new) The method of claim 49, wherein the living animal body is selected from children, the elderly, patients with hepatic and/or renal insufficiency, patients receiving treatment that induces hepatic or renal organ and/or tissue toxicity, patients receiving treatment for a heart condition, patients receiving treatment that induces cardiovascular side-effects, patients having a history of cardiovascular disease and/or suffering from cardiovascular disorders.
69. (new) The method of claim 68, wherein the history of cardiovascular disease and/or cardiovascular disorders are chosen among myocardial infarct, cardiac rhythm disorders (tachycardia, bradycardia, palpitations), blood pressure disorders (hypo- or hypertensive patients) and heart disease.
70. (new) A method for treating or preventing depression in a living animal body, while limiting the risks of cardiovascular disturbances and/or the risks of organ and/or tissue toxicity, which comprises administering to said living animal body:

- a) a mixture of enantiomers enriched in the (1S,2R) enantiomer of milnacipran and/or of at least one of its metabolites as well as their pharmaceutically-acceptable salts, and
- b) at least one active compound selected from the psychotropics, in particular antidepressants, and antimuscarinic agents,  
as associated products for use simultaneously, separately or staggered in time.

71. (new) The method according to claim 70, wherein the depression is selected from deep depression, resistant depression, depression in the elderly, psychotic depression, depression induced by the treatment with interferon, depressive state, manic-depressive syndrome, seasonal depressive episodes, depressive episodes related to general health status, depressive episodes related to mood-altering substances.

72. (new) A method for treating or preventing conditions or disorders by double inhibition of serotonin (5-HT) and norepinephrine (NE) reuptake, in a living animal body, while limiting the risks of organ and/or tissue toxicity, which comprises administering to said living animal body :

- a) a mixture of enantiomers enriched in the (1S, 2R) enantiomer of milnacipran and/or of at least one of its metabolites as well as their pharmaceutically-acceptable salts, and
- b) at least one other active substance selected from the active compounds that induce organ toxicity and the active compounds that induce cell toxicity, in particular hepatic and/or renal,  
as associated products for use simultaneously, separately or staggered in time.

73. (new) A method for treating or preventing conditions or disorders by double inhibition of serotonin (5-HT) and norepinephrine (NE) reuptake, in a living animal body, while limiting the risk of cardiovascular disturbances, which comprises administering to said living animal body:

- a) a mixture of enantiomers enriched in the (1S, 2R) enantiomer of milnacipran and/or of at least one of its metabolites as well as their pharmaceutically-acceptable salts, and

- b) at least one other active substance selected from the active compounds that induce cardiovascular side-effects,  
as associated products for use simultaneously, separately or staggered in time.